Gene Therapy Trial Yields Promising Outcomes

VITALS

Major Finding: Patients with NYHA stage III or IV heart failure who received gene therapy with MYDICAR had cardiovascular-related hospital stays that averaged 2 fewer days than those who received placebo.

Data Source: A phase II study of 39 patients enrolled in the CUPID trial.

Disclosures: Celladon Corp. funded the trial. Dr. Greenberg said that he had no relevant financial disclosures.

BY DOUG BRUNK

FROM THE ANNUAL MEETING OF THE HEART FAILURE SOCIETY OF AMERICA

SAN DIEGO – In a phase II study of patients with advanced heart failure, gene therapy with MYDICAR was found to be safe and was associated with benefit in clinical outcomes, symptoms, functional status, and cardiac structure.

Deficiency of the protein SERCA2a is central to the progression of heart failure, resulting in abnormal calcium transfer and impairing myocardial relaxation and contraction, Dr. Barry H. Greenberg said

MYDICAR, manufactured by Celladon Corp., is an enzyme replacement therapy that is designed to restore levels of SERCA2a. A viral vector delivers the SERCA2a gene.

The objectives of the study, known as CUPID (Calcium Up-Regulation by Percutaneous Administration of Gene Therapy in Cardiac Disease), were to evaluate safety and feasibility and to explore the activity and efficacy of MYDICAR in patients with advanced heart failure, said Dr. Greenberg, professor of medicine and director of the Ad-

vanced Heart Failure Treatment Program at the University of California, San Diego.

To be eligible for the trial, patients had to be 18-75 years old, have New York State Heart Association class III or IV heart failure caused by an ischemic or nonischemic etiology, have a maximal oxygen consumption of 20 mL/kg per minute or less, have a left ventricular fraction of 35% or less, and be on a stable, optimized heart failure regimen for 30 days.

Dr. Greenberg and his colleagues randomized 39 patients to one of three MYDICAR doses or to placebo, and all were treated via single intracoronary infusion. All patients were observed for 12 months, with primary analysis after 6 months of therapy.

CUPID's primary efficacy end point was defined as evidence of success in one of four areas: group-level analysis, individual analysis, time-to-event analysis, and duration of cardiovascular-related hospitalization analysis. All were deemed significant (*P* less than .2).

CUPID met the primary efficacy end point for high-dose MYDICAR treatment group vs. placebo in three of the four areas. In the group-level analysis, significant improvements were seen in the treatment group, compared with the placebo group, in 6-minute walk tests and end systolic volume, with no clinically significant worsening in any end point and numerical superiority to placebo in all other end points.

Improvements were seen in the treatment group, vs. placebo, in 6-minute walk tests and end systolic volume.

DR. GREENBERG

In the individual analysis, the mean efficacy "score" for the treatment was significantly greater than that of the placebo group. In the time-to-death analysis, the treatment group scored numerically better than the placebo group, but the difference was not significant.

In the duration of cardiovascular-related hospitalization analysis, the duration of stay was significantly shorter for the treatment group than for the placebo group (mean, 2 fewer days). ■